Original Article

# Circulating levels of omentin-1 in patients with breast cancer

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## Abstract

**Background:** It seems adipocytokines play an important role in breast cancer. Omentin-1 is a novel discovered plasma adipocytokine produced mainly in visceral adipose tissue. The aim of present study was to estimate. Circulating levels of omentin-1 in postmenopausal breast cancer patients as compare to healthy postmenopausal subjects.

**Materials and Methods:** This study consisted of 30 postmenopausal women with newly diagnosed breast cancer and 30 healthy postmenopausal subjects aged 45 to 70 years. Serum levels of omentin-1 were measured by enzyme-linked immunosorbent assay.

**Results:** The mean age of the case group was 54.3±8.3 years, and the control group was 50.3±3.2 years. The mean serum levels of omentin-1 in the case group were 73.1±29.7 ng/mL and in the control group were 108.8±65.4 ng/mL. The mean serum omentin-1 levels were found to be significantly lower in breast cancer patients (P=0.009). We also demonstrated the negative correlation of Omentin-1 with BMI in both groups (p=0.005), however, we did not find any association between age and serum omentin-1 levels (P=NS).

**Conclusion:** Our studied showed that Omentin-1 level was significantly reduced in the breast cancer patients as compare to healthy controls. Decreased omentin-1 levels may contribute to the development of cancer, however determination of its role and mechanisms needs more investigations. To sum up, our data suggest that omentin-1 can be used as a marker for early detection of breast cancer in postmenopausal women.

**Keywords:** Breast cancer, omentin, serum

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## Introduction

Breast cancer is the most prevalent type of cancer and leading cause of death due to all types of cancer in women all over the world. It has been reported that breast cancer accounts for 23% of all new cancer cases and 14% of all cancer deaths in 2008 (1, 2). Less than 1% of breast cancers occur in women younger than 25 years, but the incidence of breast cancer increase sharply after 30 years in whole over the world. Whole breast cancer patients in I.R. Iran are around 40 thousand and more than seven thousand patients are added to this number each year. However, data shows an increase in its incidence in recent years as most common malignancy among Iranian women. Incidence in I.R. Iran is about a decade before Countries and more than 30% of patients are under 30 years of age (3, 4). As breast

cancer prevalence is increasing rapidly. So it is important to find predictive factors for early detection. Several studies have reported that obesity and adipokines increased the risk of postmenopausal breast cancer. However the exact mechanisms of association between adipokines and cancer is not clear (5, 6).

Over the past decades adipose tissue considered as an inactive organ that can only store energy, but recently has been introduced as an important endocrine organ that produce and secrete a number of molecules with biological effects known as adipokines such as leptin, adiponectin, visfatin, resistin and omentin(6-8). Adipokines are responsible for several processes including insulin sensitivity, regulation of lipid metabolism, glucose homeostasis, food intake regulation and inflammatory responses(10). Omentin is a novel described adipokine which almost released from visceral adipose tissue and has a molecular mass of 34 kDa(11). Omentin was first discovered in 2001 while plays a substantial role in defense mechanisms in the intestinal against harmful bacteria(12). There are two types of omentin, omentin-1 and omentin-2. Although omentin-1 is the most circulating form of omentin in blood(13). There is some evidence that serum omentin-1 level is decreased in obesity and its related disease such as insulin resistance, type 2 diabetes (14-17). In vitro studies have shown that recombinant omentin-1 enhances glucose uptake in adipocytes through activation of Akt signaling(9). Recent experiments suggest that omentin-1 play an important role in angiogenesis through Akt signaling pathway and hyper activation of Akt signaling is associated with cancer pathogenesis(18, 19). Overexpression of omentin-1 in some cancers including malignant pleural mesothelioma and colorectal cancer has been reported (20-22). The aim of this study was to compare serum omentin-1 levels in postmenopausal breast cancer patients with healthy controls. To our knowledge this is the first study investigating omentin-1 levels in breast cancer patients.

# Methods

Our study population included 30 newly diagnosed invasive breast cancer patients (stage IB) referred to ayatollah khansari hospital, Arak, I.R.Iran and 30 healthy women (control group). None of the patients received adjuvant chemotherapy or radiotherapy before sample collection. Healthy women were collected from participants in breast screening program. Inclusion criteria in both groups were as follows: postmenopausal women aged 45 to 70 years, BMI within the range of 18.5–25 kg/m2 and without any special diet. Exclusion criteria in both groups were as follows: aged below45 and above 70 years, BMI within the range below 18.5and above 25 kg/m2, special diet, menopausal women, smoking and any other metabolic diseases. As BMI may change omentin-1, so other exclusion criteria in both groups were BMI below 18.5 and above 25 kg/m2, Blood samples were collected from all participants and centrifuged at 3000 rpm for 5 minutes. Serum samples were stored at -70 degrees until analysis. Serum omentin-1 concentrations were measured by human Elisa kit (Bioassay technology laboratory, Shanghai, China) with a measurement range of 2-600 ng/L, sensitivity of 1.03 ng/L. The Intra-assay CV and Inter-assay CV were less than 8 and 10%, respectively. Informed consent obtained from all subjects before participating in the study. It should be noted the Ethics Committee of Arak University of Medical Sciences approved the study.

**Statistical Analysis.** Statistical analysis were performed with SPSS version 16.0, data were presented as mean ± SD. Student T-test was used to compare the case and control groups in a parametric way. Two –tailed test, a p value of less than 0.05 were considered as statistically significant.

# Results

This study was performed with 30 newly diagnosed invasive breast cancer patients stage IB (Group 1) and 30 female control subjects (Group 2). All subjects were postmenopausal married women which were non-smokers and non-drinkers. Furthermore, patients group had no other diseases. The mean age of case and control groups was 54.3±8.3 and 50.3±3.2, respectively. The demographic information of the groups were compared and shown in Table 1.

Patients had a mean body mass index of 24.4± 0.6 versus 23.4 ± 1.5 of control group. The omentin-1 levels in the control group were significantly higher

**Table 1.**The demographic data obtained from the questionnaires for the two groups of women.

| Groups | Mean of age ± SD (years) | Education | | | Married | OCP Consumption | Tobacco usage | Family history | |
|---|---|---|---|---|---|---|---|---|---|
| | | High | Bachlor | Primary | | | | positive | negative |
| case | 54.3 ± 8.3 | 0% | 10% | 90% | 100% | 80% | 0% | 17% | 83% |
| control | 50.3 ± 3.2 | 10% | 80% | 10% | 100% | 47% | 0% | 7% | 93% |

**Table 2.** The comparison of serum omentin-1 level and BMI between Breast Cancer Patients and control group.

| Groups | Number of Subjects | Mean of BMI ± SD ($Kg/m^2$) | Mean of omentin-1 ± SD (ng/ml) | P Value |
|---|---|---|---|---|
| case | 30 | 24. 4 ± 0.6 | 73.1 ± 29.7 | 0.009 |
| control | 30 | 23.4 ± 1.5 | 108.8 ± 65.4 | |

BMI= Body Mass Index. P value of < 0.05 were considered as statistically significant

than those in the patients group (108.8 ± 65.4 ng/ml vs. 73.1 ± 29.7 ng/ml). We also demonstrated the negative correlation of Omentin-1 with BMI in both groups (p=0.005), however we did not find any association between age and serum omentin-1 levels. The serum omentin-1 level and BMI of the groups were compared and shown in Table 2.

# Discussion

The association between obesity and cancer has been reported by several studies (21-25). Although the exact mechanism is unclear but adipocytokines such as omentin-1 considered as one possible mechanism linking obesity and cancer. Measurement of their serum levels may be early diagnostic markers for several types of cancer. Omentin-1 is a recently discovered adipokine which is inversely correlated with BMI and type 2 diabetes (26, 27).

In our study, serum omentin-1 level of breast cancer group was significantly lower than the control group (p<0.05). Furthermore, significant inverse association between serum omentin-1 levels and BMI was observed (p<0.05), however there was no association between age and omentin-1 levels (p=NS). It has been reported that there is an inverse association between circulating omentin-1 levels with proinflammatory cytokines such as TNF-α and IL-6 and also omentin-1 levels reduced in synovial fluid of patients with rheumatoid arthritis (17, 28). It has been shown that circulating omentin-1 level in patients with prostate cancer is higher than patients with benign prostatic hyperplasia, however there was no association between omentin-1 levels with cancer invasiveness (23). In another study serum omentin-1 level of patients with colorectal cancer was significantly higher than the control group and some studies indicated effect of omentin-1 on angiogenesis through Akt signaling pathway. It has been shown activation of Akt signaling play a critical role in progression of colorectal cancer through increasing cell proliferation and prevent apoptosis (18, 19, 21). However, we have not been able to confirm their results but in agreement with our findings, another study have shown lower serum omentin-1 levels in patients with renal cell cancer than the control group (24). There is some evidence that shown treatment with omentin-1 induced apoptosis in hepatocellular carcinoma cells and unregulated p53 and p21 levels. Moreover treatment with omentin-1 led to increasing protein bax/bcl2 ratio and activation of caspase-3 signaling pathway(25).

There is controversy in the correlation between serum omentin-1 levels with cancer and these different results might be due to different study population, type of cancer, cancer treatment such as chemotherapy and radiation therapy or other unknown factors that may influence omentin-1 level. There is also contradictory evidence about omentin-1 levels and BMI. Some studies have reported inverse association between omentin-1 levels and BMI but were similar between obesity and lean groups in another study(26, 29). In the current study we found that patients with breast

cancer had lower circulating levels of omentin-1 in comparison with healthy subjects and there is significant negative association between omentin-1 levels and BMI, but no association was observed between omentin-1 levels and age.

## Conclusion

Relatively small sample size was the major limitation of the present study, so further study with larger sample and more precise selection of study population is required to evaluate serum omentin-1 levels in breast cancer patients and compare with healthy controls. In conclusion, low serum omentin-1 level might be associated with creation of breast cancer. Further investigations are required to find the relation and detailed mechanisms of omentin-1 in breast cancer development.

## Conflicts of Interest

None declared

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